

NASA 14 Day Undersea Missions: A Short-Duration Spaceflight Analog for Immune System Dysregulation?

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BACKGROUND

Spaceflight-associated immune dysregulation occurs during spaceflight and may represent specific clinical risks for exploration-class missions. An appropriate ground analog for spaceflight-associated immune dysregulation would offer a platform for ground evaluation of various potential countermeasures. This study evaluated the NASA Extreme Environment Mission Operations (NEEMO), consisting of 14 day undersea deployment at the *Aquarius* station, as an analog for this phenomenon. Given the comparatively short duration, NEEMO is viewed as a Space Shuttle analog. For this study, assays included measures of adaptive immunity, viral reactivation and stress factors. Sixteen Aquanauts from missions NEEMO-12, 13 and 14 participated in the study.



AQUARIUS

- Seafloor depth: 62 feet
- Operating depth (on stilts): 47 feet
- Interior pressure: ~2.5 Atos; ambient pressure hab
- Main living space: cylinder 43 ft. x 9 ft.
- Mission durations: up to 2 weeks
- Saturation diving conditions: 17 hour decompression required for surface return
- Aquanauts: up to 6-9 hours diving per day

METHODS

A total of 16 subjects participated in this study, representing the NEEMO 12, 13 and 14 missions. Informed consent was obtained from all subjects, and relevant institutional CPHS/IRB approvals were obtained.

All NASA general immune and viral assessment methods used for this study were performed as previously described: *Aviation and Space Environmental Medicine, 2009 May, 80(5 Suppl): A37-44.*

ASSAYS

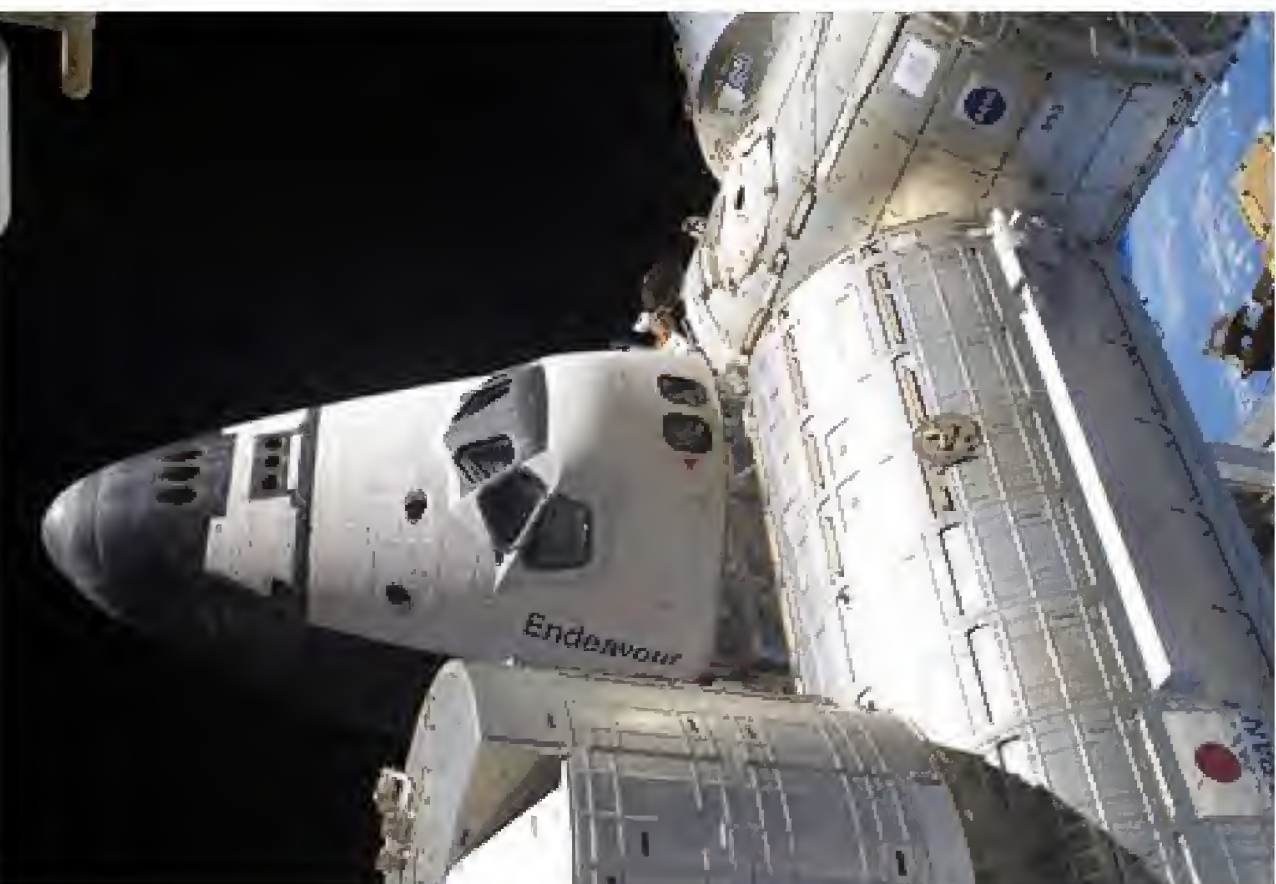
(ESA)
PMN number, function, bactericidal
In-vitro DTH
Apoptosis/necrosis
Cellular mRNA expression
Plasma purine markers of inflammation/hypoxia
Erythropoietin activity
Stress test
Stress hormones
Components of exhaled air

(NASA)
VirLeukocyte subsets*
T cell function*
Intracellular/secreted cytokine profiles*
us specific T cell number/function
Latent herpesvirus reactivation
Circadian rhythm analysis

*data included in this presentation

SAMPLING SCHEDULE

	PRE MISSION						UNDERSEA														POST MISSION							
BLOOD (20.5 ml)	X																				X							
LIQ. SALIVA (1-2 ml)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DRY SALIVA (<1.0 ml)	X																				X							
EXHALED AIR	X																				X	X	X	X				
JSC HEALTH SURVEY	X																				X							
ESA STRESS SURVEY	X	X																			X	X	X	X				
ESA SPIELBERGER SURV.	X																				X							
	6	5	4	3	2	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14/0	1	2	3	4	5	6	7	8
	L-						Mission Day-														R+							



Analogous?

Figure 1: Location of Aquarius Station, exterior photograph

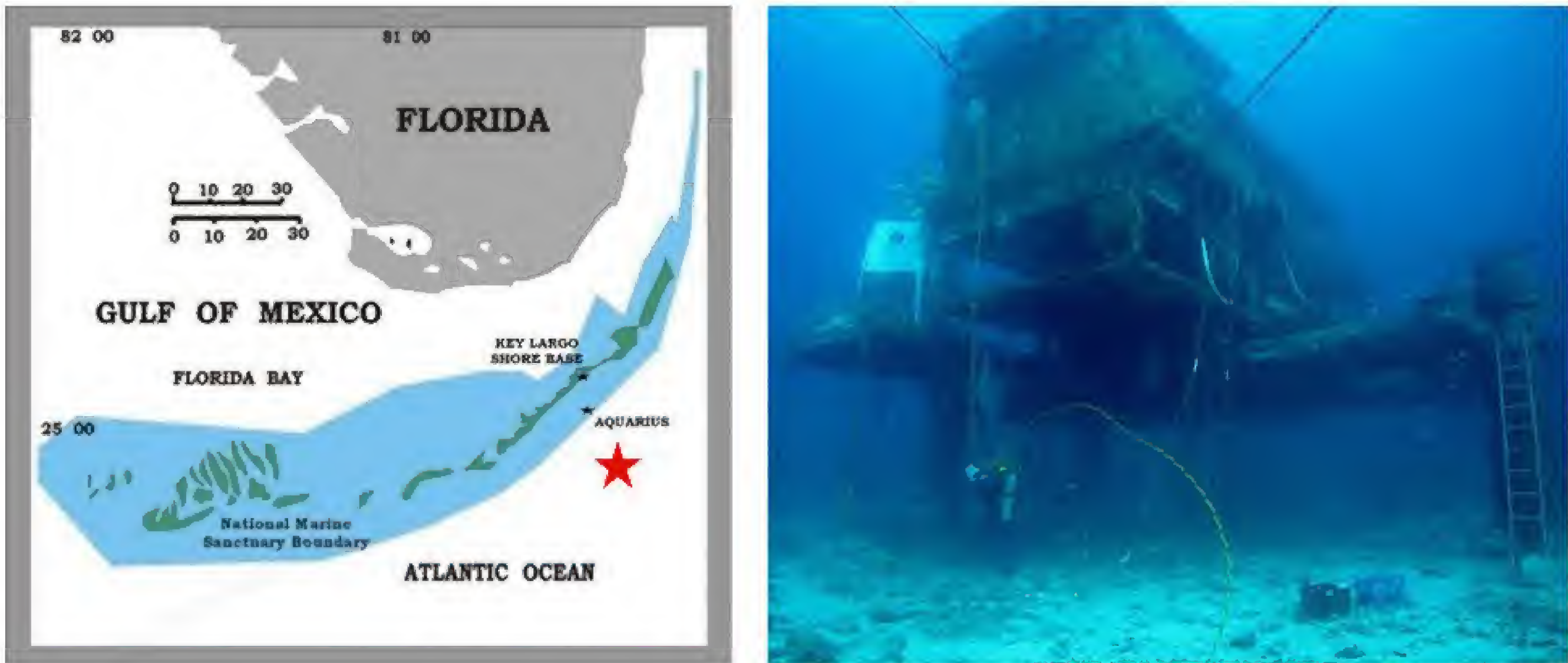


Figure 2: Mean Perinheral Leukocvte Subsets (n=16)

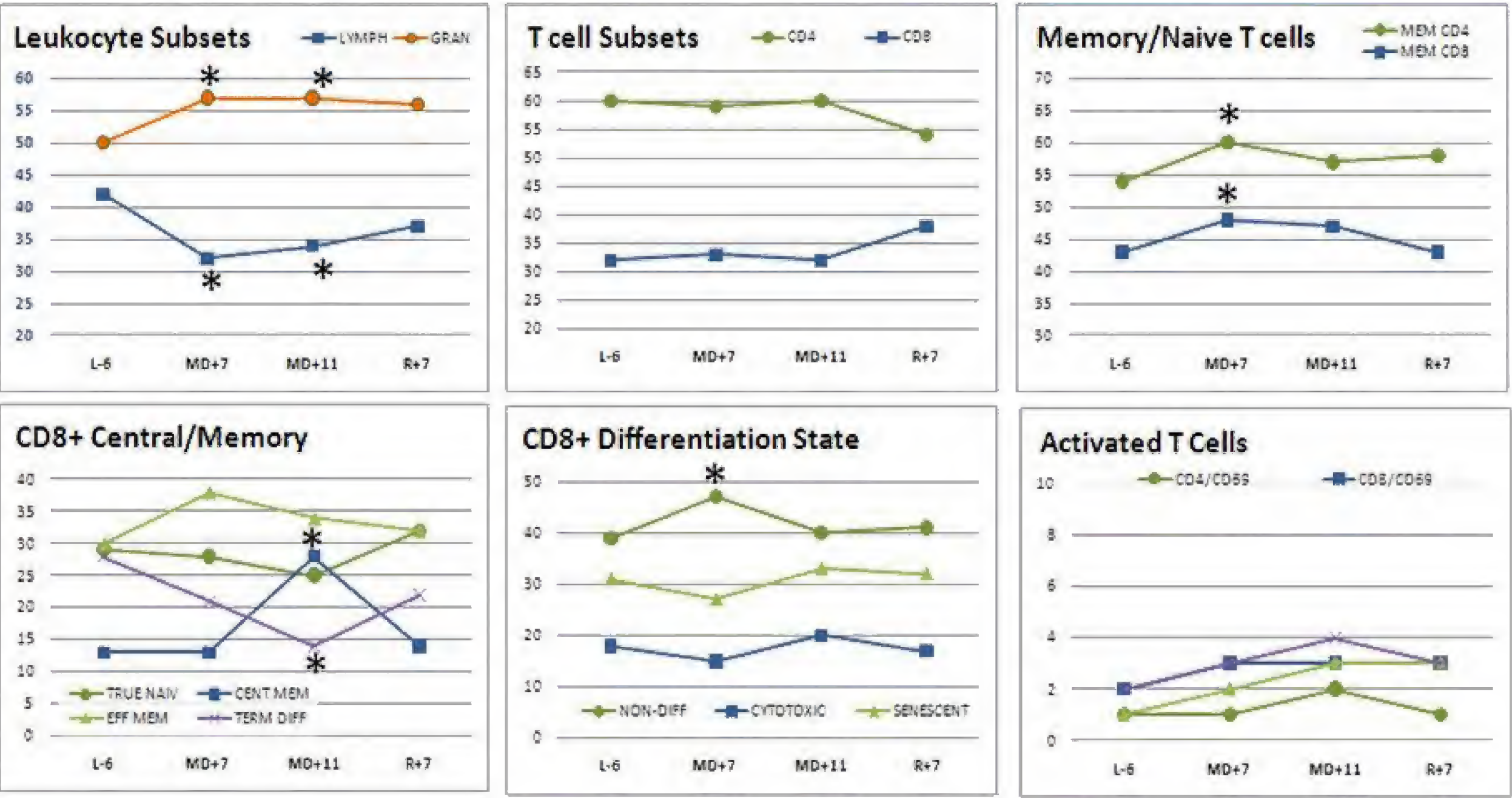


Figure 3: Individual Crew Data, Selected Functional Parameters (n=16)

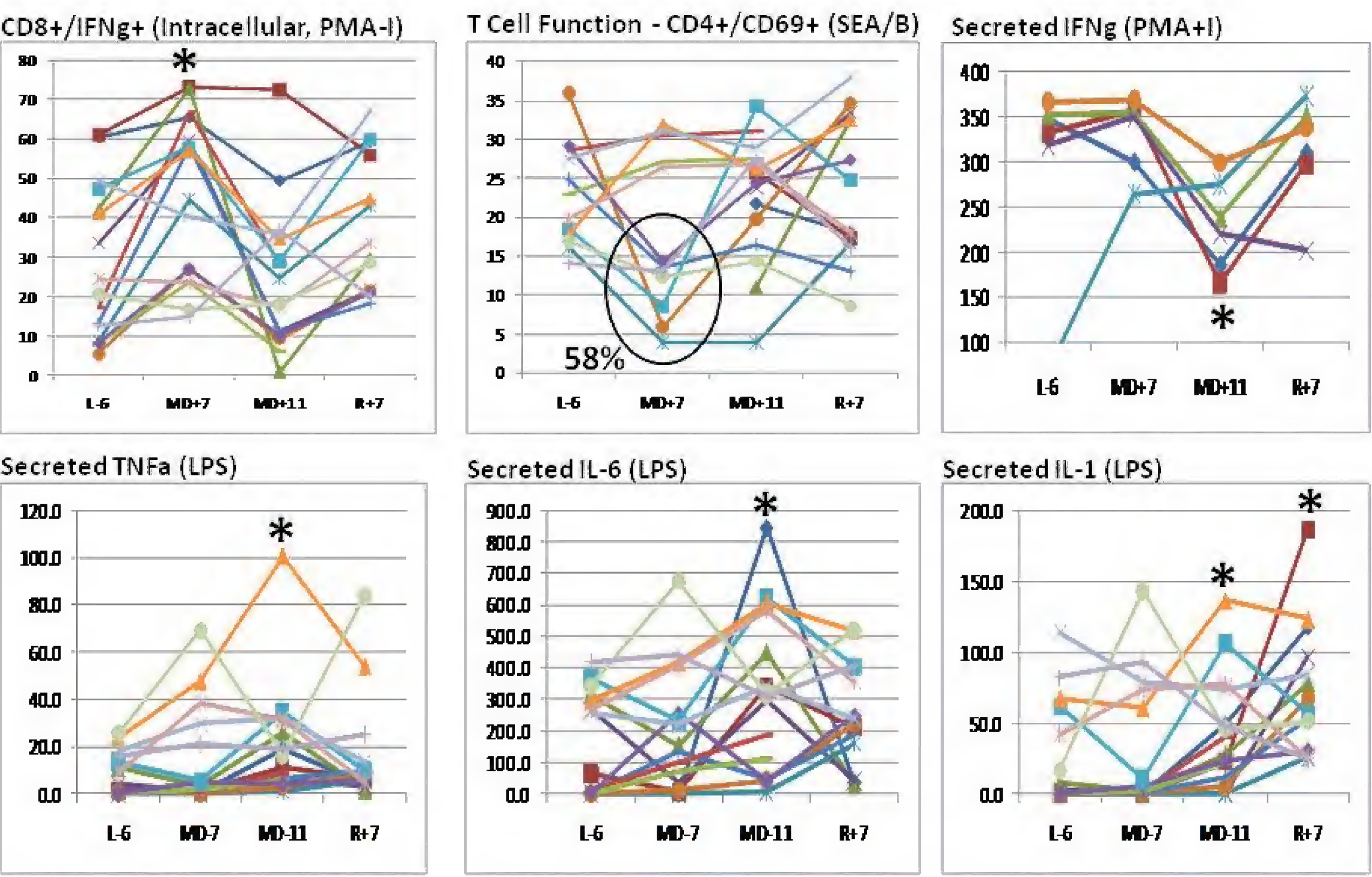


Figure 4: Virus-Specific Immunity, Cortisol, NfκB (n=16)

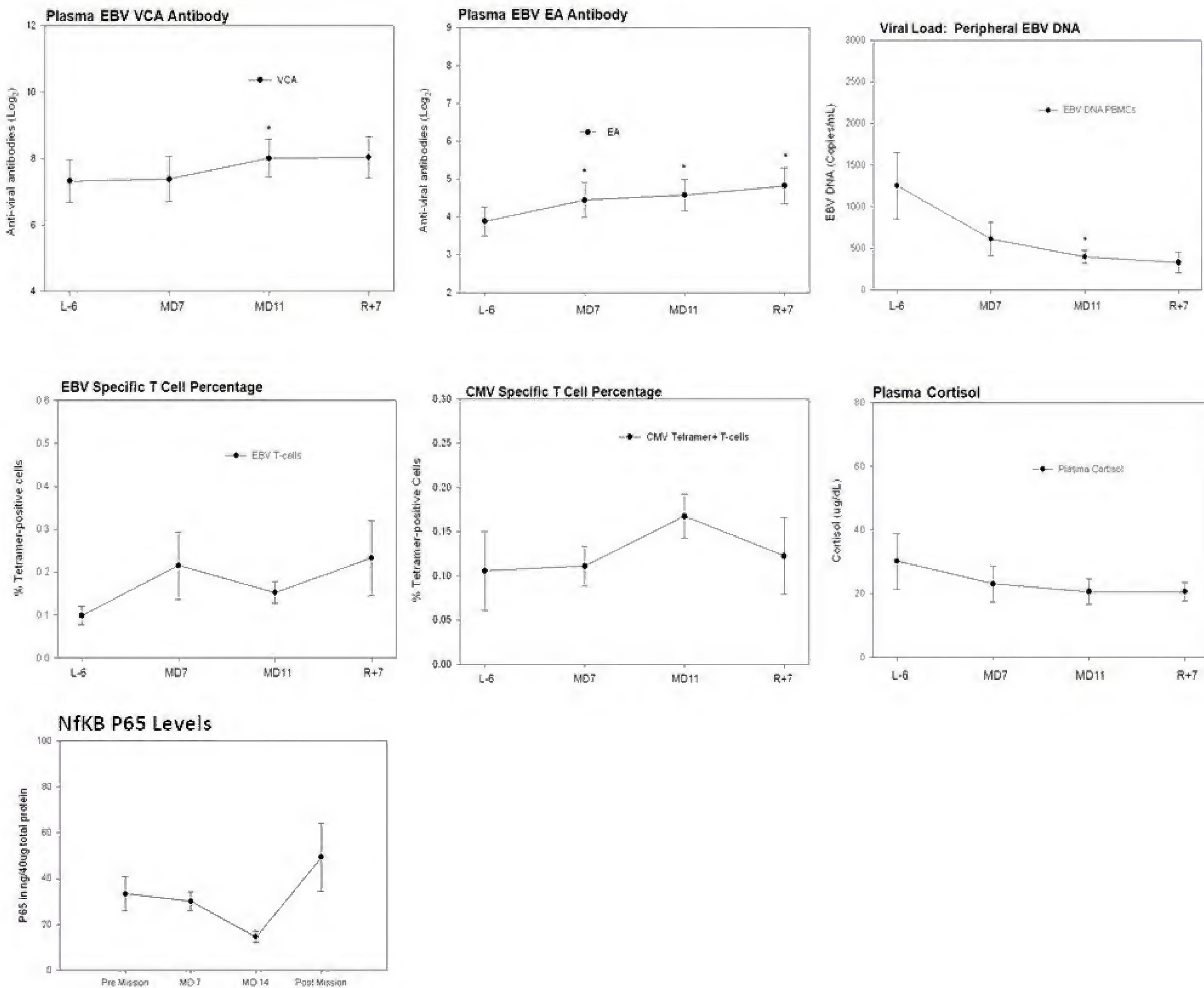
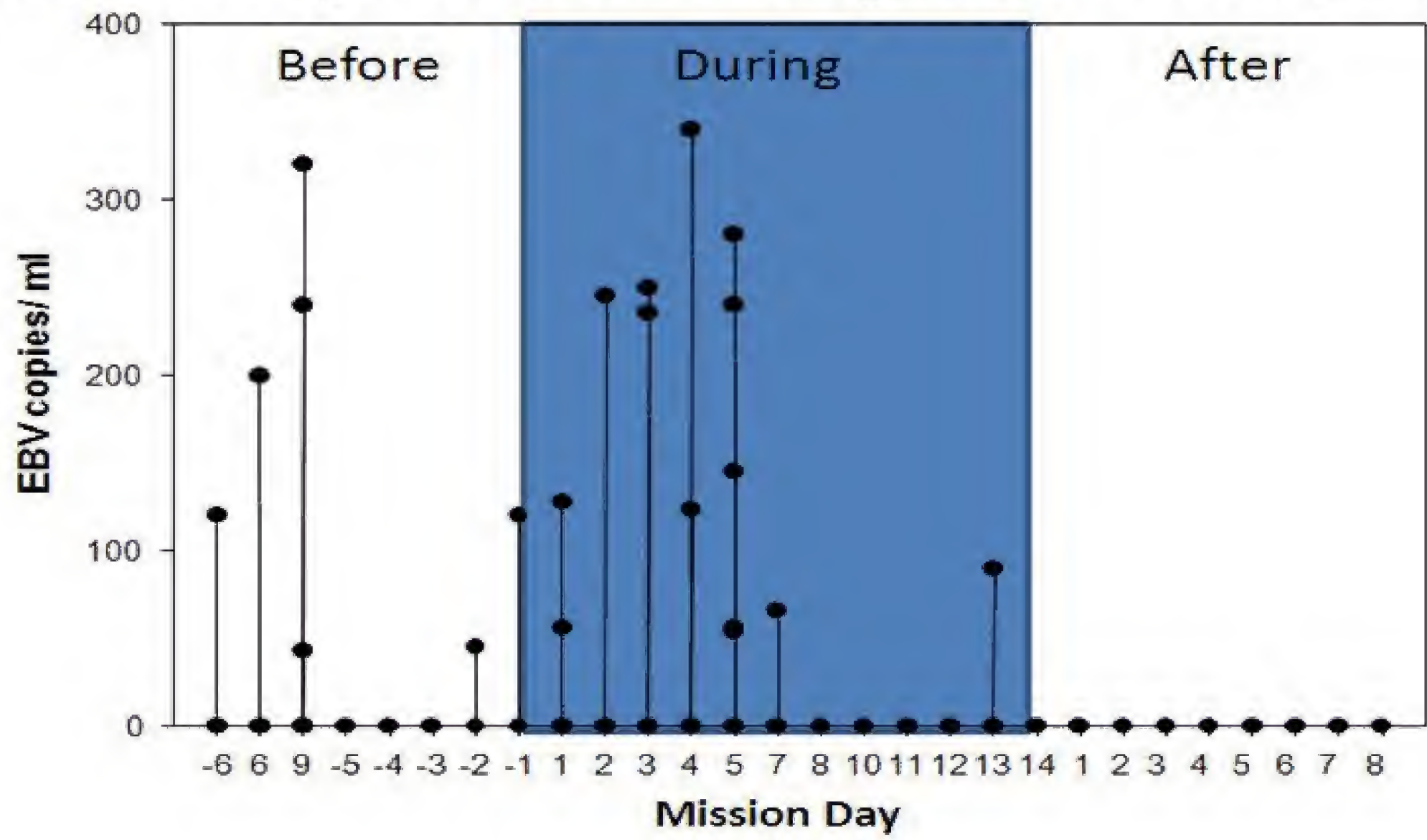


Table 1: Crewmembers with Reactivation of Latent Herpesvirus during NEEMO Missions (n=16)

	L-6	During	R+8
EBV	3	8	0
VZV	0	2	0
CMV	0	0	0

Figure 5: Shedding of EBV in Saliva during NEEMO Missions (n=16)



RESULTS

Mid-mission alterations leukocyte distribution occurred, including granulocytosis, elevated memory T cells, CD8+ T-cells subsets, constitutively activated T cells (Figure 1).

General T cell function was reduced during NEEMO missions in roughly 50% of subjects. Although the percentage of T cells secreting IFNγ rose, the bulk production declined by MD11. Production of several inflammatory cytokines rose during NEEMO missions. (Figure 2).

Assuming R+7 to be the appropriate baseline: T cell production of IFNγ, IL-5, IL-10, IL-2, TNFα and IL-6 were all reduced before and during the mission. Conversely, monocyte production of TNFα, IL-10, IL-6, IL-1b and IL-8 were elevated during mission, more so at the MD-14 time point (data not shown).

Granulocyte adhesion molecule expression (e.g. CD11b, CD62L) as assessed in NEEMO-14 indicated high activation during mission (data not shown).

Antibodies to Epstein-Barr virus (EBV) viral capsid antigen and early antigen were increased in approximately 40% of the subjects (Figure 4).

Changes in EBV tetramer-positive CD8+ T-cells exhibited a variable pattern. Antibodies against Cytomegalovirus (CMV) were marginally increased during the mission (Figure 4).

Herpesvirus reactivation was determined by PCR. EBV viral load was generally elevated at L-6 (Figure 4). Higher levels of EBV reactivation were found before and during the NEEMO missions (Figure 5), VZV reactivation occurred in 2 NEEMO crewmembers, no CMV reactivation was observed in any of the NEEMO mission or control samples (Table 1). Plasma cortisol was elevated at L-6.

CONCLUSION

Some changes in leukocyte distribution, T cell function, cytokine production, virus specific immunity and viral reactivation that occur during NEEMO missions are similar to those observed during or immediately following spaceflight.

Unfortunately, 6 days prior may be too near to mission start to serve as an appropriate baseline measurement.

The NEEMO platform may have utility for short-duration, ground-based spaceflight-immune research, such as investigations of mechanism or countermeasures validation.

